| **Advisory Action Before the Filing of an Appeal Brief** | **Application No.** 10/759,526 | **Applicant(s)** GEORGE ET AL. | |
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| | **Examiner** Janet L. Epps-Ford | **Art Unit** 1633 | |

***--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --***

THE REPLY FILED 05 November 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on *15 November 2007*. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☒ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: *See Continuation Sheet*. (See 37 CFR 1.116 and 41.33(a)).
4. ☒ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1-3,5-15,17-28 and 63-86*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____
13. ☒ Other: See Continuation Sheet.

/Daniel M. Sullivan/
Primary Examiner
Art Unit 1636

Continuation of 3. NOTE: Independent claims 1, 15, 24-28, 63-64 and 85-86 are drawn to methods and have been amended to include the phrase "and wherein said cell is part of a gastrointestinal tissue, synovium or lung tissue". The scope of the claims has been further limited by an amendment that was not previously presented. This limitation requires additional search and consideration. In addition, the amendment raises new issues under 112, second paragraph, as the amended base claims provide no antecedent for cell types such as epidermal melanocyte, hair follicle papilla cell or skeletal muscle recited in the dependent claims.

Continuation of 11. does NOT place the application in condition for allowance because: Once a final rejection that is not premature has been entered in an application, applicant or patent owner no longer has any right to unrestricted further prosecution. The amendments do not place the application either in condition for allowance or in better form for appeal. For reasons given above, and on the grounds that the amended claims raise further issues for consideration which would require an additional search of the prior art, the amended claims have not been entered. Applicant is invited to review MPEP 714.12.

Continuation of 13. Other: Claims 17-19 have been amended to correct dependency on the proper base claim 15.

Claims 1-3, 5-15, 17-28 and 63-86 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an in vitro method of acceleration of the cell cycle in fibroblasts using radio frequency radiation, in vitro method of activation of a cell cycle regulator, a signal transduction protein, a transcription factor, a DNA synthesis protein and a receptor in fibroblasts and keratinocytes using radio frequency radiation, does not reasonably provide enablement for an in vivo method for accelerating the cell cycle, comprising delivering to a cell an effective amount of any type of electromagnetic energy, or enablement for an in vivo method for activating a cell cycle regulator, signal transduction protein, transcription factor, DNA synthesis protein or a receptor in vivo, or enablement for an in vivo method for inhibiting an angiotensin receptor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

This rejection is maintained for reasons given the Office Action mailed 5/3/2007 and for reasons outlined below. In the previous Office Action, In re Gardner, Roe and Willey, 427 F.2d 786, 789 (C.C.P.A. 1970) was cited for the proposition that the law requires Applicants' disclose how to use the claimed invention. Applicants submit that the Gardner case involved disclosure of rat dosages to enable treatment in human and enablement was lacking because the court found that human doses are likely to vary hugely from effective doses in rats. Applicants submit that the rats are not accepted models for correlating human dosages. Applicants also submit that the Simko and Mattson reference cited in the present Office Action clearly confirms that in vitro results are accepted in the art as reasonably correlating to in vivo results by using the in vitro data regarding cellular changes in response to electromagnetic field exposure as a basis to draw a variety of conclusion about in vivo effects and should be accepted as evidence for the enablement of the in vivo embodiments of the invention.

Applicants submit that in the case cited by The Johns Hopkins Univ. v. CellPro, Inc., 152 F.3d 1342, 47 U.S.P.Q.2d 1705 (Fed. Cir. 1998), the Federal Circuit clearly stated that routine experimentation does not constitute undue experimentation:
The test [for undue experimentation] is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed.
Id. (Emphasis added) (citing PPG Indus., Inc. v. Guardian Indus. Corp., 75 F.3d at 1564, 37 U.S.P.Q.2d at 1623); see also In re Wands, 858 F.2d at 736-40, 8 U.S.P.Q.2d at 1403-07.

Applicants submit that for the reasons set forth in Applicants' previous response, it is submitted that the cited references confirm that the enabled in vitro working examples are recognized by those skilled in the art as correlating to in vivo conditions. Applicants submit that the Office has cited passages of these references that imply that some experimentation may be necessary by the skilled person to practice the methods. If this is the case, Applicants submit that it does not defeat enablement nor does it change the fact that the references confirm the art acceptance of in vitro results as correlating to in vivo results.
Applicants submit that unless the Office produces particular evidence to the contrary, the acknowledgement that in vitro methods are enabled should be accepted as evidence for the enablement of the in vivo embodiments of the invention. In view of the extensive teachings and working examples as previously discussed on the record; the Office's acknowledgement that the in vitro methods are enabled and the evidence those skilled in the art accepted the correlation between in vitro and in vivo results for the claimed methods, it is respectfully submitted that the enablement rejection is not properly supported.

Applicant's arguments filed 11/5/2007 have been fully considered but they are not persuasive. Applicant's main argument appears to be that the in vitro working examples provided by the specification support the enablement of the in vivo embodiments, based on arguments in The Johns Hopkins Univ. v. CellPro, Inc.,. and Simko and Mattson (of record).
However, enablement is based on evaluation of a combination of factors including scope of the claims, state of the art, unpredictability of the art, amount of guidance provided, working examples, nature of the invention and level of skill in the art.
Although the specification does disclose an in vitro example of delivering radio frequency energy to chemically synchronized primary human fibroblasts and epidermal keratinocytes, the claimed methods encompass a much broader scope. The genus of the type electromagnetic energy to be administered is very broad and the scope of the proteins to be activated in order to activate a complex process such as the cell cycle is extremely broad.

With regard to guidance in the specification, the instant disclosure provides guidance regarding intensity and duration of energy for administration of radio frequency energy to an in vitro cell culture. The specification does not provide any guidance regarding the in vivo administration of radio frequency energy or any other type of electromagnetic energy. The specification does not provide guidance regarding the administration of an effective amount of electromagnetic energy to cells to accelerate the cell cycle in vivo when the cell cycle of cells has not been synchronized. The specification does not provide guidance regarding the acceleration of the cell cycle for any other cell besides fibroblasts. The specification does not provide guidance regarding administration parameters for any other type of electromagnetic energy in vivo or in vitro so that an effective amount would be delivered in order to accelerate the cell cycle or activate a cell cycle regulator, a signal transduction protein, a transcription factor, a DNA synthesis protein, a receptor or inhibit an angiotensin

receptor. The specification does not provide guidance regarding how to determine an effective amount of any of the claimed types of electromagnetic energy for specifically activating a cell cycle regulator.

Although the citation from Johns Hopkins v. Cellpro states that a considerable amount of experimentation is permissible, it also stipulates the condition that the experimentation is merely routine, or that the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed. In this case, the instant specification does not provide a "reasonable amount of guidance" to enable the determination of how to practice a desired embodiment of the invention claimed without excessive and undue trial and error experimentation. Methods of this kind are not routine and are known in the art to be unpredictable, as taught by Simko and Mattsson. In response to the Applicants' request for particular evidence to the contrary, the Wands analysis of the Forman factors previously presented by the Examiner and discussion herein represents evidence that the in vivo embodiments are not enabled,
The scope of the claimed methods is very broad, the methods are not routine, there are art recognized issues in delivering electromagnetic energy to an in vivo complex tissue and the working examples and guidance provided by the specification do not provide a sufficient basis for the skilled artisan to be able to make or use this invention without undue trial and error experimentation.

It appears that Applicants have presented arguments and amended the claims to include the phrase "said cell is part of a gastrointestinal tissue, synovium, or lung tissue" in order to overcome the prior art rejections of the claims under 35 USC 102(b) and 102(e). However, the proposed amendments will not be entered and therefore, the arguments are not relevant to the claims as filed on 1/29/2007.

Laura McGillem Mitchell
Examiner
11/21/2007